REMARKS

Claims 1-45 are pending in the application. Claims 10-14, 18, 21, and 23-45 are withdrawn. Claims 1-9, 15-17, 19, 20, and 22 are currently under examination. Claims 1, 3, 15, and 17 have been amended. Claims 2, 4-6, and 16 have been canceled. Claims 46 and 47 have been added. Upon entry of the present amendment, claims 1, 3, 7-9, 15, 17, 19-20, 22, and 46-47 will be under examination. Support for the new claims and amendments to the original claims may be found in the original specification as filed. No new matter has been added.

Amendment of the claims or cancellation of any claims should in no way be construed as an acquiescence, narrowing, or surrender of any subject matter. The amendments are being made not only to point out with particularity and to claim the present invention, but also to expedite prosecution of the present application. Applicant reserves the option to prosecute the originally filed claims further, or similar ones, in the instant or subsequently filed patent applications.

Objection to the drawings

The Examiner has objected to the drawings. In response, Applicant respectfully submits 8 sheets of Replacement Sheets for Figures 1-7B. Applicant respectfully submits that the Replacement Sheets submitted herewith do not include new matter. Reconsideration and withdrawal of this objection is respectfully requested.

Rejections under 35 U.S.C. § 102

Claims 1-6 stand rejected under 35 U.S.C. § 102(e) as allegedly being anticipated by Bonjouklian et al. (U.S. Pat. No. 5,504,103). More specifically, the Examiner states:

> Bonjouklian et al., teach methods of treating phosphatidylnositos-3-kinase (*sic*) dependent conditions in a mammal comprising contacting the cell with wortmannin or wortmannin analog (col. 14-16, claims 1-20). While Bonjouklian et al.,teach the exact same method step as the instant claims (i.e. contacting cells with wortmannin), Bonjouklian et al. do not expressly teach contacting T cells or specifically T cells with express a CD28 receptor with wortmannin. Bonjouklian

> et al., also do not expressly teach the modulation of T cell proliferation or modulation of lymphokine production. However, it is inherent in the methods taught by Bonjouklian et al., that the administration of wortmannin or wortmannin analogs to a mammal results in the inhibition of phosphatidylinositol 3-kinase in any and all cells in mammals which express phosphatidylinositol 3-kinase.

Applicant expressly traverses this rejection. However, merely for expediting prosecution, claim 1 has been amended to recite a step of providing a T cell for which inhibition of T cell activation is desired. Applicant believes that this amendment obviates the rejection of these claims. As indicated by the Examiner, Bonjouklian et al. do not expressly teach contacting T cells or specifically T cells with express a CD28 receptor with wortmannin. Also as indicated by the Examiner, Bonjouklian et al., also do not expressly teach the modulation of T cell proliferation or modulation of lymphokine production. The step of providing a T cell for which inhibition of T cell activation is desired is therefore neither expressly nor inherently taught by Bonjouklian et al. Thus, reconsideration and withdrawal of this rejection is respectfully requested.

Rejections under 35 U.S.C. § 112, first paragraph

Claims 15-17, 19-20, and 22 stand rejected under 35 U.S.C. § 112, first paragraph for allegedly lacking enablement. More specifically, the Examiner states:

> [T]he specification does not reasonably provide enablement for claims directed to a method of inducing unresponsiveness to an antigen in a T cell and further administering the T cell to a subject suffering from an autoimmune disease. . . The specification provides insufficient data to enable claims directed to the method as broadly claimed. Thereby, specific issues including treatment of a complex autoimmune disorder associated with abnormal immune responses have to be examined to be considered for patentability regarding the broadly claimed methods.

Applicant respectfully traverses this rejection. Factors to be considered by the Examiner in determining whether it would require undue experimentation to practice the claimed invention include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art,

(7) the predictability or unpredictability of the art, and (8) the breadth of the claims. The specification teaches a number of different diseases and conditions upon which the inhibition of an immune response may be used to treat those diseases and conditions. Thus, one skilled in the art after reading the specification would recognize that the inhibition of the activity of phosphatidylinositol 3-kinase to downregulate an immune response would be advantageous in a variety of diseases, including the treatment of autoimmune diseases such as rheumatoid arthritis, psoriasis, multiple sclerosis, and Crohn's disease (see, e.g., the paragraph bridging pages 9-10 of the specification).

The Examiner has relied heavily on the unpredictability of the art in support of this rejection. Applicant, however, respectfully submits that it would not require undue experimentation based on the amount of direction or guidance presented in the specification, the working examples in the specification, and the relative skill of those in the art to determine whether a given disease falls within the scope of the claims. A considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed. (See MPEP 2164.06.)

In determining whether a given disease falls within the scope of the claims, the T-cell response of individuals suffering from a disease (e.g., in response to an antigen) may be compared to the T-cell response of normal healthy individuals (e.g., in response to the same antigen). A difference in the respective T-cell responses indicates that inducing unresponsiveness to an antigen in a T cell of a diseased individual, via the claimed invention, to reflect that of the healthy individual, will be therapeutic for the diseased individual, and thus that the disease of the individual falls under the scope of the present invention. Applicant respectfully submits that it would not require undue experimentation to practice a method for inducing unresponsiveness to an antigen in a T cell as claimed. Thus, reconsideration and withdrawal of this rejection is respectfully requested.

Claim rejections under obviousness-type double patenting

Claims 1-9 stand rejected under the obviousness-type double patenting as being unpatentable over claims 1-4 and 7-10 of U.S. Pat. No. 6,632,789. Applicant respectfully

requests that this rejection be held in abeyance until claims of the instant application are otherwise deemed allowable.

CONCLUSION

Early and favorable consideration of the application is respectfully solicited. The Examiner may address any questions raised by this submission to the undersigned at (617) 832-1000. If any fees are due, the Commissioner is hereby authorized to credit any overpayment or charge any deficiencies to **Deposit Account No. 06-1448, WYS-014.02**.

Dated: July 18, 2007

Customer No.: 25181

Respectfully submitted,

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